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Mechanisms of Maxillomandibular Advancement Surgery in the Management of Obstructive Sleep Apnea

Obststructive sleep apnea (OSA) is a common disorder characterized by recurring episodes of airflow reduction (hypopnea) or cessation (apnea) during sleep due to pharyngeal collapse. The prevalence of OSA in Canada is estimated to have increased from three to six per cent between 2009 and 2017 and is likely underreported (1-3). OSA is a major risk factor for numerous neurobehavioural and cardiovascular complications, the most common of which include excessive daytime sleepiness, hypertension, heart failure, and stroke (4-6). Considering the morbidity and mortality associated with OSA, effective long-term management is critical.

OSA can be diagnosed using polysomnography, a sleep study that monitors obstructive respiratory events among other parameters. The number of events per hour make up the apnea-hypopnea index (AHI), which determines the severity of OSA (mild: $AHI > 5$, moderate: $AHI \geq 15$, severe: $AHI \geq 30$) (2). OSA can be treated non-surgically using continuous positive airway pressure (CPAP) therapy; however this approach requires consistent use of an external ventilator and patient compliance is often poor (7). Surgical interventions that primarily remodel soft tissue in the throat (i.e. tonsillectomy, uvulopalatopharyngoplasty) have had limited success (8-10). Maxillomandibular advancement (MMA) has been shown to be an effective treatment modality indicated for OSA patients who have difficulty tolerating CPAP or who are refractory to other interventions (11-14).

The MMA procedure consists of a Le Fort I osteotomy and bilateral sagittal split osteotomy with rigid internal fixation (Figure 1, bottom left). The combined effect of these bony alterations is increased tension on muscles and other soft tissues; this is thought to result in expansion

of the naso-, oro-, and hypopharyngeal airways (Figure 1) (11). The exact mechanism by which MMA improves the obstructed airway has been a subject of study since the early 2000s and remains poorly understood. The aim of this article is to summarize the current state of research investigating mechanisms through which MMA changes airway morphology to improve OSA outcomes.

Effect of MMA on pharyngeal airway morphology

Poiseuille's law states that the resistance of an incompressible Newtonian fluid in laminar flow through a tube is directly proportional to the tube's length and inversely proportional to the fourth power of the radius (Figure 2). This relation is widely applied in medicine and is frequently cited as the endpoint upon which MMA acts (15-20). Numerous studies have used cephalometry to analyze changes in airway morphology associated with MMA; however the two-dimensional nature of this technique imparts major limitations (17,21). For this reason, the present review will focus on research leveraging computed tomography (CT) or magnetic resonance imaging (MRI) to allow a comprehensive analysis of n-dimensional parameters (Figure 3, Table 1). It should be noted that MMA is often performed alongside a counter-clockwise rotation (CCWr) of the maxillomandibular complex, to enhance the facial contours of class II (retrognathic) patients and allow for greater advancement distances without excessively decreasing the nasolabial angle (18). It is also common for a genioglossal advancement (GA) to be performed concomitantly, for cosmetic and/or functional reasons (22). Unfortunately, many studies investigating three-dimensional changes to the airway after surgery do not dis-

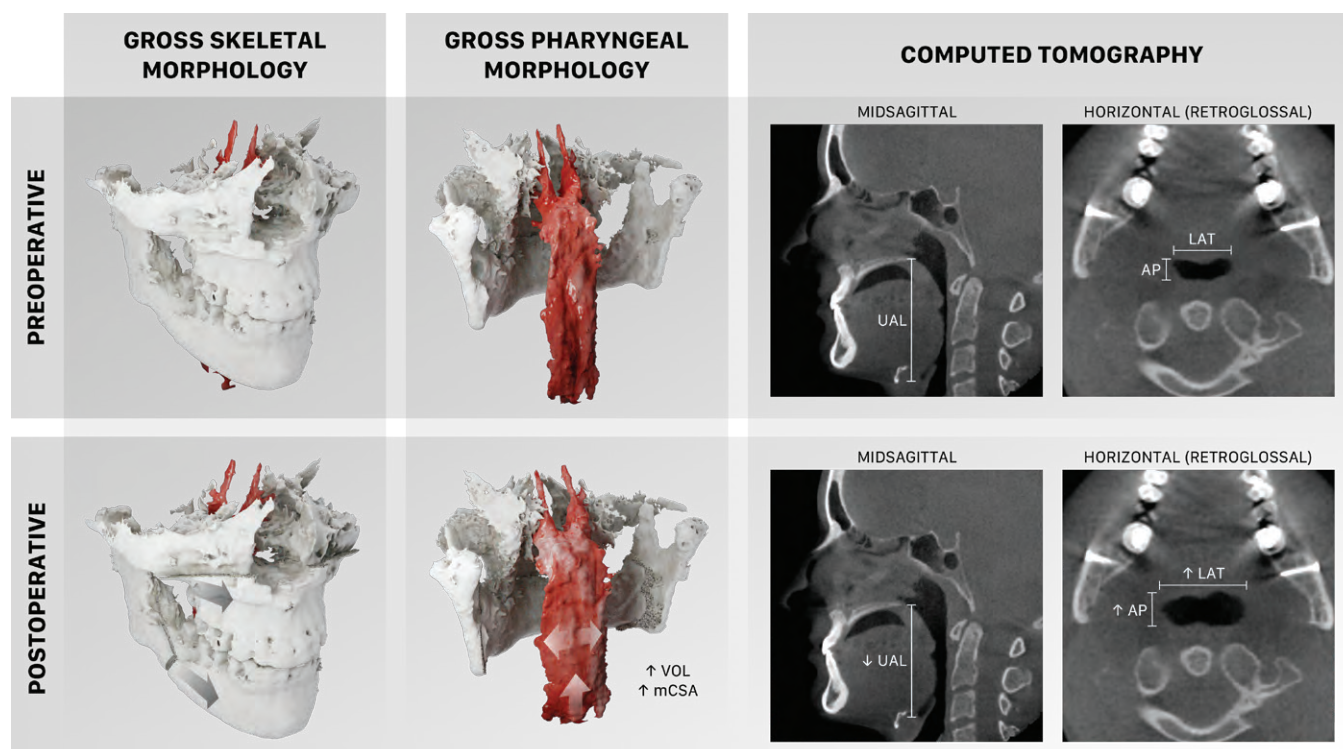


Figure 1. Three-dimensional models and simulated cone beam computed tomography scans of skeletal and pharyngeal morphology before and after MMA. Abbreviations: VOL, total airway volume; minCSA, minimum horizontal cross-sectional area; UAL, upper airway length; AP, anteroposterior dimension at minCSA or retroglossal airway; LAT, lateral dimension at minCSA or retroglossal airway; ↑, increased in magnitude; ↓, decreased in magnitude.

tinguish between MMA alone, MMA + CCWr, and MMA + GA, potentially confounding the cause-effect relationship (19-21,23,24).

In 2010, Susarla et al. established that upper airway length (UAL) is a strong predictor of OSA, with high sensitivity and specificity (27). An UAL ≥ 72 mm was found to be associated with a 19-fold increase in odds of having OSA compared to an UAL < 72 mm. Although a class II craniofacial profile is common in OSA patients, it is not consistently associated with increased UAL and is thus not a reliable predictor of OSA pathogenesis (27). MMA was found by numerous studies to decrease UAL significantly, thus contributing to reduced airway resistance according to Poiseuille's law (16-20,25). Abramson et al. suggested that even small increases in an airway cross-sectional area can be magnified by a reduced UAL, since resistance along a single conduit is added in series (17,18). However, in contrast to the findings of Susarla and Abramson, Butterfield et al. found no significant difference in UAL between preoperative OSA patients and healthy controls (55.81 vs. 56.14 mm) (19). This suggests a high UAL may not necessarily be pathognomonic for OSA (19).

The ratio of mediolateral (LAT) and anteroposterior (AP) airway dimensions has been shown to predict severity of OSA (33). Most studies show a high LAT:AP (more elliptical) to be favourable and closer to physiological dimensions found in healthy individuals, while OSA patients have a consistently lower LAT:AP (more circular), in addition to narrower and longer airways (17,19). For instance, a retrospective study of 15 OSA patients reported an increasing respiratory distress index (RDI) with increasing airway length and decreasing LAT:AP (17). While MMA increases the absolute magnitude of both LAT and AP dimensions, it has also been shown to have an effect on LAT:AP (22,34). Counterintuitively, MMA produces a larger increase in LAT dimensions compared to AP (22). Brown et al. speculate that this occurs via an aponeurotic connection from the lateral ramus of the mandible to the lateral walls of the nasopharynx (35). The pterygomandibular raphe (PR) was identified as a likely candidate based on tagged MRIs of 30 healthy subjects undergoing simulated mandibular advancement using an occlusal splint (35). In brief, the anterior movement of the mandible during MMA is thought to apply tension to the lateral pharyngeal wall

PREOPERATIVE**POSTOPERATIVE****POISEUILLE'S LAW**

$$R = \frac{8\eta L}{\pi r^4}$$

R = Resistance

η = Dynamic viscosity

L = Length of tube

r = Radius of tube

Figure 2. A visual representation of Poiseuille's law and how MMA decreases airway resistance.

via the PR, thus decreasing extraluminal tissue pressure, decreasing lateral airway compliance, and reducing the risk of collapse (35-38). Others have suggested that absolute airway dimensions have a greater impact on collapsibility than relative dimensions. For instance, Butterfield et al. studied the airway morphologies of 12 pre- and postoperative patients and found no significant difference in LAT:AP (19). However, the absolute magnitudes of LAT and AP were found to be significantly smaller in postoperative OSA patients and healthy controls when compared to pre-

operative OSA patients (19). The effect of LAT:AP on OSA remains controversial (17,19).

Total pharyngeal airway volume (VOL) and minimum horizontal cross-sectional area (minCSA) are currently the two most investigated airway morphologic parameters in the literature (39-41). A meta-analysis demonstrated a significantly smaller VOL in preoperative OSA patients compared to postoperative OSA patients (40). Several studies also showed VOL is significantly lower in preoperative OSA patients compared to healthy controls (16,18,19,24-

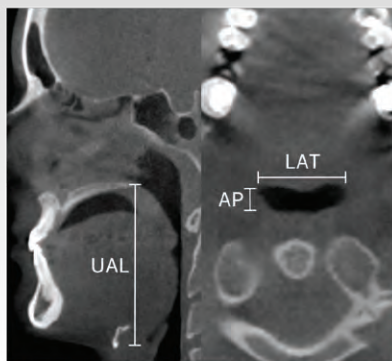
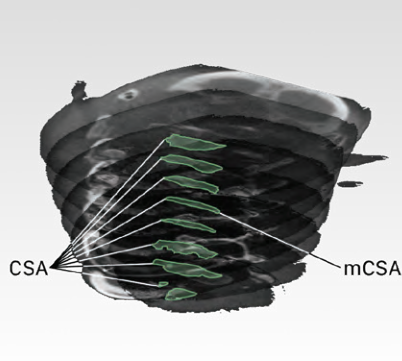
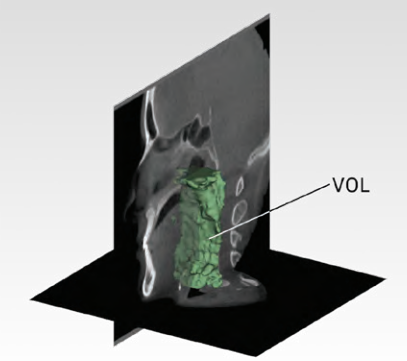
1-DIMENSIONAL METRICS**2-DIMENSIONAL METRICS****3-DIMENSIONAL METRICS**

Figure 3. A visual summary of one, two, and three-dimensional parameters/metrics used for evaluating the effect of MMA on pharyngeal airway morphology. Abbreviations: UAL, upper airway length; AP, anteroposterior dimension at minCSA or retroglossal airway; LAT, lateral dimension at minCSA or retroglossal airway; CSA, horizontal cross-sectional area; minCSA, minimum horizontal cross-sectional area; VOL, total airway volume.

Table 1. Airway morphologic parameters of preoperative, postoperative, and control patients collected from primary literature involving OSA patients treated with MMA.

PARAMETER	STUDIES	PREOPERATIVE OSA		POSTOPERATIVE OSA		CONTROL (non-OSA)	
		Mean $\pm$ SD	n	Mean $\pm$ SD	n	Mean $\pm$ SD	n
UAL	Butterfield et al.,(9) 2015	55.81 $\pm$ 5.51	12	48.52 $\pm$ 7.05 *	12	56.14 $\pm$ 7.41	12
	Butterfield et al.,(0) 2015	57.03 $\pm$ 6.25	15	49.83 $\pm$ 7.94	15	–	–
	Hsieh et al.,(25) 2014	72.8 $\pm$ 3.72	16	69.7 $\pm$ 3.63	16	–	–
	Gonçalves et al.,(26) 2013	59.7 $\pm$ 2.33	30	-4.76 $\pm$ 2.27 (Δ)	23	–	–
	Abramson et al.,(16) 2011	74.8 $\pm$ 6.5 *	11	70.7 $\pm$ 7.8 **	11	66.3 $\pm$ 10.1	17
	Susarla et al.,(27) 2010	74.3 $\pm$ 7.3 ***	96	–	–	63.5 $\pm$ 5.9	56
LAT	Butterfield et al.,(9) 2015	16.73 $\pm$ 5.17 *	12	23.98 $\pm$ 5.11	12	21.70 $\pm$ 5.14	12
	Butterfield et al.,(0) 2015	15.93 $\pm$ 5.73	15	23.89 $\pm$ 4.90	15	–	–
	Gonçalves et al.,(26) 2013	23.82 $\pm$ 1.95	30	2.11 $\pm$ 1.73 (Δ)	23	–	–
	Abramson et al.,(16) 2011	26.0 $\pm$ 6.7 *	11	31.6 $\pm$ 4.5 **	11	22.3 $\pm$ 7.7	17
AP	Butterfield et al.,(9) 2015	4.33 $\pm$ 2.34 *	12	10.60 $\pm$ 3.69 **	12	6.68 $\pm$ 2.03	12
	Butterfield et al.,(0) 2015	4.37 $\pm$ 2.24	15	10.71 $\pm$ 3.55	15	–	–
	Gonçalves et al.,(26) 2013	7.88 $\pm$ 0.74	30	-2.08 $\pm$ 1.6 (Δ)	23	–	–
	Abramson et al.,(16) 2011	10.3 $\pm$ 3.9	11	14.6 $\pm$ 6.0 *	11	10.9 $\pm$ 4.1	17
LAT:AP	Butterfield et al.,(9) 2015	4.64 $\pm$ 2.62	12	2.58 $\pm$ 1.38	12	3.43 $\pm$ 0.84	12
	Butterfield et al.,(0) 2015	4.38 $\pm$ 2.67	15	2.53 $\pm$ 1.33	15	–	–
	Gonçalves et al.,(26) 2013	3.13 $\pm$ 0.31	30	0.8 $\pm$ 0.36 (Δ)	23	–	–
	Abramson et al.,(16) 2011	2.7 $\pm$ 0.7 *	11	2.5 $\pm$ 0.9 *	11	2.4 $\pm$ 1.4	17
minCSA	Butterfield et al.,(9) 2015	82.56 $\pm$ 52.70 *	12	247.38 $\pm$ 104.92 **	12	141.68 $\pm$ 61.38	12
	Butterfield et al.,(0) 2015	79.09 $\pm$ 51.98	15	247.24 $\pm$ 100.45	15	–	–
	de Sousa Miranda et al.,(28) 2015	107.9 $\pm$ 35.7	23	184.5 $\pm$ 43.9	23	–	–
	Schendel et al.,(22) 2014	76.3 $\pm$ 25.4 (RP)	10	253.2 $\pm$ 70.8 (RP)	10	–	–
	Schendel et al.,(22) 2014	98.6 $\pm$ 28.4 (RG)	10	182.2 $\pm$ 51.1 (RG)	10	–	–
	Hsieh et al.,(25) 2014	110 $\pm$ 49	16	190 $\pm$ 58.8	16	–	–
	Raffaini & Pisani,(29) 2013	157.7 $\pm$ 54.0	10	295 $\pm$ 80	10	–	–
	Gonçalves et al.,(26) 2013	78.46 $\pm$ 17.7	30	63.7 $\pm$ 33.3 (Δ)	23	–	–
	Abramson et al.,(16) 2011	60.5 $\pm$ 39.3 *	11	196.2 $\pm$ 136.6 *	11	73.9 $\pm$ 39.2	17
VOL	Butterfield et al.,(9) 2015	9.68 $\pm$ 3.81 *	12	17.4 $\pm$ 7.51	12	13.5 $\pm$ 4.4	12
	Butterfield et al.,(0) 2015	9.72 $\pm$ 3.65	15	17.5 $\pm$ 7.19	15	–	–
	de Sousa Miranda et al.,(28) 2015	20.4 $\pm$ 3.0	23	30.5 $\pm$ 3.9	23	–	–
	Schendel et al.,(22) 2014	4.1 $\pm$ 1.1 (RP)	10	10.41 $\pm$ 2.92 (RP)	10	–	–
	Schendel et al.,(22) 2014	4.7 $\pm$ 1.3 (RG)	10	9.2 $\pm$ 2.1 (RG)	10	–	–
	Hsieh et al.,(25) 2014	17.1 $\pm$ 3.53	16	23.2 $\pm$ 4.21	16	–	–
	Bianchi et al.,(30) 2014	12.9 $\pm$ 2.48	10	20.7 $\pm$ 2.17	10	–	–
	Raffaini & Pisani,(29) 2013	15.256 $\pm$ 4.02	10	22.623 $\pm$ 4.55	10	–	–
	Valladares-Neto et al.,(31) 2013	13.8 $\pm$ 1.4	25	21.6 $\pm$ 1.7	25	–	–
	Gonçalves et al.,(26) 2013	8.70 $\pm$ 1.15	30	3.93 $\pm$ 1.59 (Δ)	23	–	–
	Abramson et al.,(16) 2011	12.8 $\pm$ 5.1	11	20.6 $\pm$ 8.7 **	11	12.3 $\pm$ 4.6	17
	Hernández-Alfaro et al.,(32) 2011	14.532 $\pm$ 3.16	10	23.799 $\pm$ 5.1	10	–	–

Abbreviations: UAL, upper airway length (mm); LAT, lateral dimension at minCSA or retroglossal airway; AP, anteroposterior dimension at minCSA or retroglossal airway; LAT:AP, LAT to AP ratio; minCSA, minimum axial cross-sectional area (mm²); VOL, total airway volume (cm³); RP, retropalatal; RG, retroglossal; Δ , change in parameter (preoperative – postoperative).

All P values are in relation to the control group. P < 0.05 (*), P < 0.01 (**), P < 0.001 (***).

26,29,30,42). Class II craniofacial profiles are not consistently associated with low VOL (19). In terms of retropalatal and retroglossal mCSA, an inverse correlation exists with RDI (43). A meta-analysis on patients undergoing MMA + CCWr showed a significant increase in VOL and mCSA, while another meta-analysis showed similar results after MMA alone (21,23). Healthy individuals often have a retroglossal mCSA, while preoperative OSA patients generally have a retropalatal mCSA (22,44). MMA increases VOL by 237 per cent on average, acting disproportionately on the retropalatal region (22). This causes a mCSA to migrate from retropalatal to retroglossal (22). The enlargement of VOL is likely precipitated by increased tension on suprahyoid and velopharyngeal musculature attached to the bony structures altered by MMA (22,34,35). Brown et al. have also demonstrated that mandibular advancement causes *en bloc* anterior movement of the tongue, another potential contributor to increased VOL (35). Compared to other airway morphologic parameters, the connection between low VOL and OSA appears to be more consistent in the literature, potentially due to the metric's higher dimensionality in relation to mCSA, UAL, LAT, and AP.

Ongoing research and clinical relevance

Airway morphological factors are highly relevant for the success of MMA and should be analyzed using cone beam CT preoperatively, to precisely plan the amount of maxillary or mandibular advancement required. However, there is still a need for optimal advancement distances (ADs) to be defined (31,46-49). Currently an AD of 10 mm is widely used in clinical practice based on recommendations made by Riley et al. in a retrospective study that showed an inverse correlation between mandibular AD and RDI (31,41,46,49,50). Since then, other studies have recommended ADs greater than 10 mm, and various others have shown significant increases in VOL with significantly lower AD (31,40,51). Recently, a proof-of-concept study examined how advancing the maxilla and mandible in two mm increments affects airway morphology. Wolak et al. found that maximum incremental change (MIC) of VOL and AP occurs at four mm, while MIC of LAT occurs at 10 mm (47). However, a contrasting study found MIC of LAT occurs during early MMA (two to six mm) (48). Further research is necessary to understand the incremental relationship between AD and airway morphology. This would allow surgeons to manage OSA while minimizing alteration to the facial profile, achieving a more functional and esthetic result.

The effects of MMA on airway morphology are also varied due to inherent anatomical variations between individuals. One such example is the pterygomandibular raphe (PR), an aponeurotic connection between the bucci-

nator and superior pharyngeal constrictor that is absent in 36 per cent of the population (52). Considering the putative role of the PR in lateral expansion of the oropharynx during MMA, it is reasonable to hypothesize that its congenital absence would affect key tissue properties, such as compliance (35). The specific mechanistic and clinical implications of these types of anatomical variations should be further investigated.

Despite the strong association between airway morphology and OSA outcomes, some patients have residual symptoms after MMA (19). This is likely a result of the multifactorial pathophysiology of OSA, involving non-anatomical factors such as sleep position, obesity, medications, and low arousal threshold (17,53). The neurological derangements of OSA remain poorly understood (54,55).

Conclusion

MMA can be used to manage moderate to severe cases of OSA in patients refractory to CPAP and other treatments. MMA is a surgical intervention that acts upon several key airway morphological parameters (VOL, mCSA, UAL, LAT, AP), which has been shown to improve patency, reduce airflow resistance, and ameliorate polysomnography outcomes (AHI, RDI) (16,19,25,27,33,41). Only with a comprehensive understanding of the relationship between anatomical changes and medical outcomes can researchers improve upon existing MMA techniques and develop next-generation therapies for OSA patients. 

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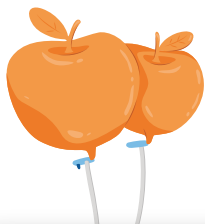
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